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fever is obtained, there should be made a careful bacteriologic examination of the urine and several specimens of stool to determine the presence or absence of typhoid bacilli. The stools must be obtained with the aid of a cathartic or the findings are more likely to be negative, even though the person is a chronic carrier. More trustworthy results could, no doubt, be obtained by making a bacteriologic examination of the duodenal contents, but the facilities for procuring the specimen are generally not at hand in the average country village and small city.

THE EFFECT OF FEEDING YEAST ON ANTIBODY PRODUCTION

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This work has been undertaken in the attempt to discover the effect of feeding yeast on antibody formation in the rabbit, with the view to a possible explanation of the therapeutic value claimed for yeast in infectious diseases.

From the time of Hippocrates until the present day, yeast has been used as a therapeutic agent in diseases, particularly in those of an infectious nature. Hippocrates used it in the local treatment of leukorrhea, and later it was used by the uncivilized tribes of France and Germany in the same way. Clinicians in the second half of the last century were interested in both its use and its mode of action, and we find articles in regard to yeast, its dosage and its action in various diseases, appearing intermittently from the time of Mosse[1] in 1852, to the present work of Hawke[2] and his associates. The French clinicians in the last years of the last century and the early years of the present, were particularly interested in its mode of action, and such men as Landau, Beylot, Petit, Nobécourt, and others worked on the problem, but obtained no positive results. Hypotheses in abundance were forthcoming, but the true mode of action was unknown. Debousy[3] postulated a "vaccine" secreted against the microbe of furunculosis. Landau[4] thought there might be a threefold action: a direct cellular antagonism, a mechanical expelling of the organisms causing the disease by the overgrowth of the yeast, and finally the use of substratum for its own benefit to the detriment of the other organisms. Beylot[5] attributed an antiglycemic rôle to yeast. De Backer and Jacquin gave it a phagocytic activity, while Calmette proved that it had no such powers. Petit held that yeast could have no antiseptic power, for all those substances with this power suppress the fermentation of yeast; so that he thought that the most important factor was the vegetable nature of yeast, the fact that it takes up enormous quantities of carbon dioxid and renders the atmosphere toxic for the aerobic bacteria. Vigier[6] considered ferments, vegetable nature, growth, and all other suggestions unimportant, and he believed that some other substance, an alkaloid for instance, was the substance to which the action of yeast in disease was to be attributed. On the other hand, Coirre[7] said that the therapeutic activity was always proportional to the

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[1] Lancet, 1852, 2, p. 113.

[2] Jour. Am. Med. Assn., 1917, 69, p. 1243.

[3] Jour. de méd. et de chir. prat., 1894, 65, p. 476.

[4] Jour. de méd. et de chir. prat., 1896, 67, p. 274.

[5] Thése de Bordeaux, 1896.

[6] Revue de thérap. méd.-chir., 1900, 67, p. 152.

[7] Revue de thérap. méd.-chir., 1900, 67, p. 82.

energy of the ferment, which remained the sole criterium to serve as a guide, since it is unknown whether the therapeutic value resides in the act of fermentation, or whether the presence of the ferment per se, fighting the germs that it meets, has the desired effect. Nobécourt[8] suggested the possibility that other as yet unknown substances might be the true active principles of yeast, but concluded that the vital action of the vegetable was the really important action. Bolognesi[9] did not believe that the zymases themselves were important, but that there was some soluble ferment not precipitated by the alcohol which was the true active portion. Brocq[10] finally concludes that yeast acts as a "modifier of the general state, active enough to render the ground unfavorable for the development of the staphylococcus, but not a specific for it." Lardier[11] has shown that as yet no conclusion has been reached by the French school. Hawke and his co-workers have emphasized the efficacy of yeast in the treatment of furunculosis and other staphylococcus infections. They have given no explanation for its action, but suggest that the laxative value combined with some fixed effect on the intestinal tract may be the cause of improvement that follows its use.

Since all the diseases for which yeast is said to be a specific are induced by staphylococcus, streptococcus, and other pyogenic organisms, and since the recovery from these diseases is due to an increased antibody production, it is logical to suspect that yeast, if it has any beneficial action, has an influence on the yield in antibodies. In order to find if this is so, we studied the effect of the feeding of yeast on the production of antibodies to sheep blood cells in rabbits. We had in mind, also, the possibility of discovery and isolation of a substance which specifically increases the production of antibodies, an accomplishment not yet attained, but the importance of which has been realized in clinical medicine. The experiment has been made three times with a series of new animals each time.

Six full-grown rabbits were used each time, two as controls; four were fed with yeast. The controls were fed as much carrots and oats as they desired. The remaining rabbits were placed in individual cages, and each of them fed daily half a cake of Fleischmann's compressed yeast mixed with ground carrots, and after this had been eaten, as much fresh carrots and oats as the animals would eat. After the first time, this was continued for a period of approximately one month.

In the first series, each animal was injected with 30 c c of fresh whole sheep blood intraperitoneally. This was found to be toxic, so the remaining work was done with washed sheep corpuscles. In the first series, 3 to 4 c c of blood was drawn from an ear vein from each animal every 4 days until the sixteenth day, and the antibodies were titrated after each bleeding. In the table, the figures referring to "Lysin" represent the highest dilution of rabbit serum in question in which complete lysis of sheep corpuscles was produced. The tubes were incubated for 2 hours and then placed in the icebox until morning. In each test the total quantity of the mixtures was 0.6 c c, of which 0.2 c c was a 5% suspension of sheep corpuscles and 0.012 c c guinea-pig serum as complement; and the remainder rabbit serum and salt solution. Since the estimation of the lysin was made at various times, and not all at once, the figures must be regarded as only approximately correct with regard to the lysin in the rabbit serum at different bleedings because of the undoubted variations in the activity of the guinea-pig serum used as complement, and in the resistance of the sheep corpuscles employed in the different sets of tests. The results, however, are believed to be accurate enough for the requirements in this case. The figures and curve referring to "Agglutinin" give the highest dilution of rabbit serum in which there was a trace of agglutination, namely a halo around the clumped corpuscles. In the case of "Precipitin" the figure and curve refer to the highest dilution of water laked sheep blood with which the serum of the rabbits formed a definite precipitate after 1 hour at room temperature.

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[8] Jour. de méd. de Paris, 1900, 12, p. 266.

[9] Revue de thérap. méd.-chir., 1899, 66, p. 695.

[10] Presse méd. 1899, 1, p. 45; Jour. de méd. et de chir. prat., 1900, 71, 896.

[11] Thése de Paris, 1901-1902.

In the remaining experiments, the estimation of lysin and agglutinin was made at the same time so that the concentration of the complement and sheep corpuscles remained the same throughout. The precipitin tests were not made. In the second series of experiments, the animals were bled every 3 days, while in the third series, they were bled every 4 days. The same concentrations were used as in the case of the first group.

From the curves in each case it is seen that in no case is there a higher concentration of hemolysins in the yeast-fed animals than in the controls.

In Table 1 are given the results obtained with the third group of animals which fairly well represent the results obtained with the other groups.

TABLE 1

The Effect of Feeding Yeast After the Injection of Sheep Blood on the Production of Lysin and Agglutinin in Rabbits

Days after Injection of Antigen	Rabbit 1		Rabbit 4		Rabbit 5—Control		Rabbit 6—Control	
	Lysin	Agglutinin	Lysin	Agglutinin	Lysin	Agglutinin	Lysin	Agglutinin
4	0	192	12	768	6	192	6	192
8	6	1,536	12	1,536	12	3,072	12	1,536
12	12	3,072	12	3,072	24	3,072	24	12,288
16	12	192	96	6,144	96	6,144	96	12,288
20	12	384	96	6,144	96	6,144	96	12,288
24	24	768	48	1,536	96	1,536	96	3,072
28	48	384	48	1,536	48	1,536	48	192
32	0	96	12	192	12	1,537	12	192

The figures under "Lysin" give the highest dilution in which complete lysis of sheep blood was produced. The figures under "Agglutinin" give the highest dilution in which distinct agglutination was produced.

The first series shows that lysin, agglutinin and precipitin formation is greater in control animals than in yeast fed ones over a period of sixteen days. In series 2, lysin formation is considerably greater in the control than in the yeast-fed animals, but the agglutinin formation